DOI: 10.1002/jev2.12083

ISEV2021 Abstract Book

About ISEV

The International Society for Extracellular Vesicles is the leading professional society for researchers and scientists involved in the study of microvesicles and exosomes. With nearly 1,000 members, ISEV continues to be the leader in advancing the study of extracellular vesicles. Founded in 2012 in Sweden, ISEV has since moved its Headquarters to the United States. Through its programs and services, ISEV provides essential training and research opportunities for those involved in exosome and microvesicle research.

Mission Statement

Advancing extracellular vesicle research globally.

Vision

Our vision is to be the leading advocate and guide of extracellular vesicle research and to advance the understanding of extracellular vesicle biology.

ISEV2021 Annual Meeting

The International Society for Extracellular Vesicles is the is the premier international conference of extracellular vesicle research, covering the latest in exosomes, microvesicles and more. With an anticipated 1,000 attendees, ISEV2021 will feature presentations from the top researchers in the field, as well as providing opportunities for talks from students and early career researchers.

ISEV2021 International Organizing Committee

IOC Chairs: Lorraine O'Driscoll (Ireland), Sophie Rome (France)
IOC Members: Antonella Bongiovanni (Italy), Dave Carter (United Kingdom), Vincent Hyenne (France), Soazig Le Lay (France), Andreas Möller (New Zealand), Eva Rohde (Austria), Tang-Long Shen (Taiwan), Carolina Soekmadji (Australia), and Ken Witwer (USA)

Journal of Extracellular Vesicles: Editors in Chief

Jan Lotvall (Sweden)

Concurrent Sessions (CC)

CC1 | How are EVs Involved in Cancer Pathogenesis?

Chair: Hector Peinado, Spanish National Cancer Center, Spain
Chair: Lucia R. Languino, Thomas Jefferson University, United States

CC1.1 | Mitochondrial-lysosomal crosstalk induces mitochondrial-derived vesicle generation in cisplatin chemoresistance

Flora Guerra, Department of Biological and Environmental Sciences and Technologies (DiSTeBA), University of Salento
Sinforosa Gagliardi, Department of Biological and Environmental Sciences and Technologies (DiSTeBA), University of Salento
Silvia Caterina Resta, Department of Biological and Environmental Sciences and Technologies (DiSTeBA), University of Salento
Cecilia Bucci, Department of Biological and Environmental Sciences and Technologies (DiSTeBA), University of Salento

Introduction: Different studies suggest a key role of the crosstalk between mitochondria and lysosomes in cellular physiology and its dysregulation is present in cancer. Indeed, it is known that mitochondrial impairment can influence lysosomal function and viceversa. RAB7 is a small GTPase with multiple key roles in cellular physiology. RAB7 controls transport to late endocytic compartments and regulates late endocytic organelle biogenesis, lysosomal positioning and functions, trafficking and degradation of several signaling receptors and extracellular vesicle (EV) secretion. In recent works, RAB7 was described also as regulator of mitophagy, mitochondrial-lysosomal contacts and mitochondrial dynamics. Moreover, it is known that RAB7 may determine fusion between mitochondrial derived vesicles (MDVs) with late endosome, but its role in MDVs biogenesis is poorly understood.
Methods: In this context, we have purified trough ultracentrifugation and immunoisolation EVs from cisplatin chemosensitive and chemoresistant ovarian cancer cell lines. We verified their endosomal biogenesis and mitochondrial content through western blotting. Moreover, we performed PCR to analyze the presence of mitochondrial DNA (mtDNA).
Results: We found that RAB7 downregulation and impairment of late endocytic functions characterize all chemoresistant cells. Moreover, in chemoresistant cells we observed increase of EV secretion compared to matched chemosensitive cells. Interestingly, we found that purified EVs contain several mitochondrial proteins and mtDNA.
Summary/Conclusion: Here, we concluded that cisplatin chemoresistance is associated with alteration of late endocytic pathway and with consequent increase of EV secretion. It is known that cisplatin treatment induces mitochondrial dysfunction. In this context, RAB7 is not able to induce autophagic degradation of dysfunctional mitochondria which are secreted becoming potential markers of chemoresistance.

CC1.2 | The role of Notch pathway in the pro-tumorigenic activity of extracellular vesicles in multiple myeloma

Domenica Giannandrea , Università degli Studi di Milano
Michela Colombo, Università degli Studi di Milano
Natalia Platonova, Università degli Studi di Milano
Valentina Citro, Università degli Studi di Milano
Mara Mazzola, Università degli Studi di Milano
Anna Pistocchi, Università degli Studi di Milano
Raffaella Adami, Università degli Studi di Milano
Vincenza Dolo, Università degli Studi dell'Aquila
Ilaria Giusti, Università degli Studi dell'Aquila
Laura Cantone,Università degli Studi di Milano
Valentina Bollati, Università degli Studi di Milano
Mauro TurriniValduce Hospital
Raffaella Chiaramonte, Università degli Studi di Milano

Introduction: Multiple myeloma (MM) is characterized by the tight interaction between MM cells and bone barrow (BM) niche, resulting in tumor progression.
MM cells overexpressed Notch 2 and Jagged 1 and 2, triggering Notch pathway activation on BM population and their pro-tumorigenic activity.

Extracellular vesicles (EV) represent novel pro-tumorigenic players in the MM microenvironment.
In this work we assess the tumorigenic effect of MM-derived EVs and the role played by the Notch pathway in EV-mediated communication between MM cells and the BM cells.
Methods: EVs from MM cell lines (MM-EVs) or MM cell lines constitutively inhibited for Jagged1/2 (MMJ1/2KD-EVs) or Notch2 (MMN2KD-EVs) were characterized for Notch2 and Jagged1 and 2 content by Western blot and for size and number by nanoparticle tracking analysis and electronic transmission microscopy. The transfer of HA-tagged Notch2 via EVs was evaluated by an engineered system of HEK293 sending and receiving cells. Notch pathway activation was evaluated in vivo by injecting MM-EVs in the duct of Cuvier of 2 days post fertilization Notch-reporter Tg(T2KTp1bglob:hmgb1-mCherry)jh transgenic zebrafish embryos. The pro-tumorigenic effect of MM-EVs, MMJ1/2KD-EVs and MMN2KD-EVs were assessed in vitro by measuring the osteoclastogenic potential, the ability to induce human endothelial cells to organize tubular structures and assessing changes in stromal cell-mediated drug resistance.
Results: MM-EVs carry Notch2 Jagged1 and 2 and transfer them to recipient cells; Notch members levels depend on their expression in MM cells.
The analysis of the functional effects indicates that MM-EVs interact and activate Notch pathway in receiving cells in vitro and in vivo and display a pro-tumorigenic effect. MM-EVs show osteoclastogenic effect and angiogenic ability and boost drug resistance induced by the BM stromal cells HS5. All these effects are lost when EVs are produced by MMJ1/2KD and MMN2KD cells.
Summary/Conclusion: These results provide the first evidence that targeting the Notch pathway may be a valid therapeutic strategy to hamper the pro-tumorigenic role of EV in MM progression.

CC1.3 | Extracellular vesicles from triple negative breast cancer promote differentiation of pro-inflammatory macrophages associated with better clinical outcome

Mercedes Tkach, Institut Curie / INSERM U932
Jessie Thalmensi, Institut Curie / INSERM U932
Eleonora Timperi, Institut Curie / INSERM U932
Paul Gueguen, Institut Curie / INSERM U932
Nathalie Névo, Institut Curie / INSERM U932
Eleonora Grisard, Institut Curie U932
Philemon Sirven, Institut Curie / INSERM U932
Federico Cocozza, Institut Curie / INSERM U932
Alizée Gouronnec, Institut Curie / INSERM U932
Lorena Martin-Jaular,Institut Curie / INSERM U932
Mabel Jouve, Institut Curie / CNRS UMR 3215
Coralie GuérinInstitut Curie / FlowCytométrie Platform
Vassili Soumelis, Université de Paris / INSERM U976
Emanuela Romano,Institut Curie / INSERM U932
Elodie Segura,Institut Curie / INSERM U932
Clotilde Thery, MD PhD, Institut Curie / INSERM U932

Introduction: Tumor associated macrophages (TAMs) are highly abundant in human cancers, representing widely heterogeneous populations. The contribution of various tumor-derived signals to differentiation of circulating monocytes into distinct TAM subsets is not well understood. In particular, tumors release both soluble factors and extracellular vesicles (EVs: exosomes, ectosomes and others) containing a complex set of signaling molecules, whose impact on TAM precursors may be different.
Methods: Here, we used Size-exclusion chromatography (SEC) to separate EVs from soluble molecules in the secretome of triple negative breast cancer (TNBC) cell lines. We cultured human blood monocytes with EV-rich or EV-poor SEC fractions and analyzed the phenotype of differentiated monocytes in terms of cell surface marker expression and cytokine secretion, and by global transcriptomic analysis. We generated by CRISPR/Cas9 tumor cell lines KO for several genes that we identified as relevant to disclose the mechanisms mediating the observed effects (CSF1, Rab11, STING). We compared the in vitro obtained gene signatures with those of macrophages isolated from human breast tumor patients and analysed by single cell RNASeq.
Results: We show that both EVs and soluble secretome promote monocyte differentiation towards macrophages. However, EVs specifically promoted a subset of pro-inflammatory macrophages bearing an IFN signature. CSF-1 exposed on EVs was necessary for macrophage differentiation and the cGAS/STING axis was involved in the activation of the IFN-response. Macrophages imprinted with an EV-signature or with the soluble molecule signature were both found in patient's TAMs. Strikingly, EV-induced macrophage signature positively correlated with T cell infiltration and patient survival.
Summary/Conclusion: Together these data suggest that TNBC-released CSF-1-bearing EVs promote a tumor immune microenvironment associated with a favourable prognosis in TNBC patients.